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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE		
	Application Number	09/759,345
	Filing date	January 16, 2001
	Inventor	Douglas H. ROBINSON
	Group Art Unit	1645
	Examiner Name	Robert Zeman
	Attorney Docket No.	2149-107A
Tile of the Invention: METHODS FOR THE ISOLATION OF BACTERIA CONTAINING EUKARYOTIC GENES		

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TRANSMITTAL OF APPLICANT'S REPLY ON APPEAL

Dear Sir:

Enclosed in connection with the above-referenced application is the Applicant's Reply to the Examiner's Answer, in triplicate.

Respectfully submitted,

Date: May 3, 2004

Mark I. Bowditch
Reg. No. 40,315
114 S. Cherry Street
Falls Church, VA 22046
Tel. (703) 597-8785

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APPLICANT'S REPLY TO THE EXAMINER'S ANSWER

Pursuant to 37 C.F.R. § 1.193(b)(1), Applicant submits the following reply to the Examiner's Answer. Please note that a Revocation and Substitute Power of Attorney, with a change of correspondence address, has been filed concurrently herewith.

As a preliminary issue, the Examiner's Answer articulated, for the first time, specific claim language or amendments that would have been considered acceptable to overcome some of the pending rejections. Applicant regrets that such suggestions could not have been made earlier in the prosecution. Nonetheless, Applicant has filed concurrently herewith additional amendments to the claims that are believed to embody what the Examiner is suggesting in the way of claim language. Applicant respectfully requests that should these proposed amendments place the claims in condition for allowance, that they be entered in whole or in part.

First Issue: With regard to the Examiner's Answer on the First Issue (35 U.S.C. § 101 lack of utility), the Applicant again points out that the Examiner is creating an issue based on semantics where there should be none. The Examiner focuses unduly on his own conclusion that

the claim term "producing" means "creating" (as opposed to equally appropriate meanings such as "forming," "providing," "furnishing," "causing to appear," "achieving," etc. – see Roget's College Thesaurus, Random House, 2000), without regard to the abundant statements in both the specification and the prosecution history that explain that the meaning of that term as used in the claim equates with the concept of "providing" or "furnishing" ("ending up with," if you will). The Examiner insists that the discussion of "de novo speciation" in the specification equates with "creation of life" and "spontaneous generation." Answer at 5, 15. The record is clear, and Applicant again states for the record, that the term "producing" as used in the present claims does not mean the creation of life from lifeless matter, or "spontaneous generation" as that term is used in biology in reference to the theory that the Examiner correctly points out was refuted by Louis Pasteur over a century ago. It rather refers to the undeniable fact that one starts the process with cells identifiable as belonging or coming from one species (a eukaryotic cell), and ends up with cells that are identifiable as belonging to another (a bacterium). The Applicant is not claiming the creation of life, as the Examiner asserts, but rather the formation of one cell type/species from another. There is nothing in current scientific knowledge or theory to exclude the possibility of de novo speciation, and the Examiner has provided none. There are in fact well-known analogous processes whereby one life form is transformed into a radically different one, a vivid example being insect pupation, the process whereby a worm-like larvae first undergoes nearly complete cellular breakdown inside the chrysalis (cocoon), then reorganizes itself into the very different adult form of the butterfly or moth.

In the present case "de novo" (new) "speciation" (making of a species) is the best language available to describe the result achieved by the present methods. Frequently inventions deal with concepts and results for which there are no prior accepted terms, or precise definition.

In such cases a patent applicant must resort to the closest approximation available in the English language, and become his own lexicographer by precisely explaining what is meant by the term used. Such is the present situation, and the Examiner's insistence on inflexibly adhering to a definition of claim terms that is directly disclaimed and contradicted by the specification and the Applicant during prosecution, is unreasonable.

Second Issue: With regard to the Examiner's Answer on the Second Issue (35 U.S.C. § 112, first paragraph – deposit requirement), Applicant repeats that the present claims are not limited to the use of a particular starting cell line. Thus, a deposit is not necessary in order to enable the present claims, as there is adequate description in the specification of the kinds of starting materials that are suitable for use in the invention. Thirty-seven C.F.R. § 1.802(a) states that "Where an invention is, or relies on, a biological material, the disclosure may include reference to a deposit of such biological material." On their face, the claims neither are, nor rely on, a specific biological material. Thirty-seven C.F.R. § 1.802(b) states that "Biological material need not be deposited unless access to such material is necessary for the satisfaction of the statutory requirements for patentability under 35 U.S.C. § 112. ... Biological material need not be deposited, inter alia, if it is known and readily available to the public or can be made or isolated without undue experimentation." The claims recite the use of "virally infected eukaryotic cells," of which there are abundant examples readily available to the public (an few of which are specifically referenced in the specification). Furthermore, it is well within the ordinary skill in the art to make and isolate virally infected eukaryotic cells. The Examiner states that "[t]he invention appears to employ novel strains of Staphylococcus and Micrococcus." This is not so. As stated above, the claimed methods employ virally-infected eukaryotic cells. The claimed methods can produce novel strains of Staphylococcus and Micrococcus, but such strains

are not "employed" in the methods, and no claim is limited to such strains. Thus, under 37 C.F.R. §1.802, no deposit of these particular bacterial strains is required.

The Examiner asserts that "it is unclear if the starting materials were readily available to the public at the time of the invention," apparently because there is no evidence that the cell lines disclosed in the specification (and discussed at pages 14-15 of Applicant's Brief) have been *accepted* by an international depository authority. Answer at 6, 16. The Applicant fails to understand the basis for this assertion, as the cell lines in question (with one exception) are identified by their American Type Culture Collection accession numbers, so clearly they are a part of the ATCC collection and have been accepted by the ATCC, a depository authority under the Budapest Treaty. These are not the Applicant's cell lines – they are publicly-available cell lines obtained by the Applicant from the ATCC and so under the express terms of 37 C.F.R. §1.802(b) they "need not be deposited."

Third Issue: With regard to the Examiner's Answer on the Third Issue (35 U.S.C. § 112, first paragraph, enablement), Applicant's again submit that the Examiner is applying the wrong standard. The Examiner asserts that "[i]t does not appear that the claimed method would be suitable for the production of bacteria from any and all eukaryotic cells."[1] Answer, page 8. First, the first paragraph of 35 U.S.C. § 112 is satisfied if even a single means for practicing the claimed invention is enabled. Engel Industries, Inc. v. Lockformer Co., 946 F.2d 1528, ___, 20 U.S.P.Q.2d 1300, 1304 (Fed. Cir. 1991) ("The enablement requirement is met if the description enables any mode of making and using the claimed invention."). The Examiner does not dispute

[1] The Examiner's failure to specify "virally-infected" eukaryotic cells, to the use of which all of the claims are limited, is assumed to be an oversight.

that the specification enables the production of bacteria from at least the virally-infected eukaryotic cells lines detailed therein.

The question then becomes whether or not the Applicant should be required to provide specific enablement for the production of bacteria from any and all eukaryotic cells; in other words, does the specification have to enable each and every embodiment within the scope of the claim? The Federal Circuit has clearly held that the answer to this question is "no." The Federal Circuit held in In re Wands, 865 F.2d 1247, 9 U.S.P.Q.2d 1461 (Fed. Cir. 1989), that specific enablement of a single hybridoma cell line that secreted a specific antibody was sufficient to support claims to the generic class of monoclonal antibodies because those skilled in the monoclonal antibody art could, using the state of the art and applicant's disclosure, produce and screen other hybridomas secreting other monoclonal antibodies falling within the generic class.

As in the Wands case, the present application discloses the essential criteria for selecting starting materials, detailed methodology regarding how to carry out the steps of the claimed methods, and the essential criteria for screening and selecting the useful products of the methods. With the guidance provided by the specification, it is well within the ordinary skill in the art to select and culture appropriate starting cell lines, and screen the resulting cultures for the useful products of the methods (methods for identifying intact eukaryotic genes in cells are well-known in the art, for example). The fact that some virally-infected cell lines might not be suitable for use in the claimed methods does not negate enablement. In re Vaeck, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991) ("... we do not imply that patent applicants in art areas currently denominated as 'unpredictable' must never be allowed generic claims encompassing more than the particular species disclosed in their specification. It is well settled that patent applicants are not required to disclose every species encompassed by their claims, even in an

unpredictable art ..."); Atlas Powder Co. v. E.I. du Pont de Nemours & Co., 750 F.2d 1569, 224 U.S.P.Q. 409 (Fed. Cir. 1984) ("Even if some of the claimed combinations were inoperative, the claims are not necessarily invalid."); In re Angstadt & Griffen, 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976). The Examiner's objection based on undue breadth addressed in the Fuetterer case is quite similar to the Examiner's position here. In Fuetterer, 138 USPQ 217 (CCPA 1963), the Examiner had taken the position that the recitation "inorganic salt that is capable of holding a mixture of said protein and/or carbohydrate in colloidal suspension" was unduly broad and functional. The Examiner reasoned that "an organic salt" read on literally thousands of materials, many of which would not be operative for Applicant's purpose. The Examiner further stated that certain undisclosed salts had not been enabled. The CCPA resoundingly rejected the Examiner's position. "We see nothing in patent law which requires appellant to discover which of all those salts have such properties and which will function properly in his combination. The invention description clearly indicates that any inorganic salt which has such properties is usable in his combination... [H]is claims should not be so restricted that they can be avoided merely by using some inorganic salt not named by appellant in his disclosure."

The Examiner also asserts that practicing the present invention would require undue experimentation. The Examiner, however, points does not point to any aspect of the claim that requires "undue" experimentation within the meaning of the patent laws. "That some experimentation may be required is not fatal; the issue is whether the amount of experimentation required is 'undue.'" In re Vaeck, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991). In fact, § 112 first paragraph permits extensive experimentation, so long as it does not "require ingenuity beyond that to be expected of one of ordinary skill in the art." In re Angstadt, 190 U.S.P.Q. at 218. The Board of Patent Appeals and Interferences has elaborated on this definition as follows:

> "The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed."

Ex parte Jackson, 217 U.S.P.Q. 804, 807 (B.P.A.I. 1982). To the extent the Examiner's concerns relate to how the method produces the bacteria, as the Applicant explained at page 18 of the Applicant's Brief, such issues are simply not relevant if the first paragraph of § 112 is otherwise satisfied. See Newman v. Quigg, 11 U.S.P.Q.2d 1340, 1345 (Fed. Cir. 1989) (not a requirement of patentability that an inventor correctly set out, or even know, how or why the invention works); Fromson v. Advance Offset Plate, Inc., 219 U.S.P.Q. 1137, 1149 (Fed. Cir. 1983) ("it is axiomatic that an inventor need not comprehend the scientific principles on which the practical effectiveness of his invention rests.").

Fourth Issue: With regard to the Examiner's Answer to the Fourth Issue (35 U.S.C. § 112, second paragraph), the Applicant provides the following comments in addition to what is set forth in the Applicant's Brief.

Claims 1 and 15 were rejected for use of the allegedly vague language "under low oxygen conditions." Notwithstanding the express definition of this term in the specification at page 9, the Examiner maintains that this term does not clearly define the metes and bound of the claimed invention. The Examiner now in his Answer has indicated that the problem lies specifically in the failure to define an upper limit for the range. Answer at 24. The Applicant has filed concurrently herewith amendments to claims 1 and 15, such that they recite the range "0-2 v/v% oxygen," which Applicant believes embodies what the Examiner suggests in the Answer might be acceptable claim language to overcome this rejection.

Claims 2, 3 and 15 were rejected for the recitation of "subjecting the cells to an aerobic culturing step," though "they depend upon claims that require culturing under low oxygen conditions." Answer, page 11. First, claim 15 is an independent claim, and so it is unclear to the Applicant how this rejection applies to claim 15. Second, here is no inconsistency between recitation of "low oxygen conditions" and the recitation of "aerobic" conditions – they refer to different steps of the culture method, and the specification expressly defines "low oxygen conditions" as including both anaerobic conditions and "alternating anaerobic culturing conditions with at least one brief period of exposure to an aerobic or microaerophilic condition," so there can be no inconsistency in reciting such alternating conditions. See specification at page 9, lines 15-18. Claim 2 simply further defines the "low oxygen conditions" as anaerobic conditions with at least one exposure to aerobic or microaerophilic conditions. Claim 3 specifies that the cells be subjected to a further aerobic culturing step. If in the Examiner's opinion the actual words used in claims 2 and 3 do not clearly state this situation (though Applicant believes they do), the Applicant is certainly amenable to amending the claims to phase it a different way, but the Examiner has offered no guidance to suggest alternative language that he would consider satisfactory. The Amendment filed concurrently herewith attempts to address this issue by amending claim 2 to recite "anaerobic culture conditions interrupted with at least one intermediate exposure of the cells to aerobic or microaerophilic culture conditions." Applicant has already submitted a proposed Amendment After Final Rejection changing claim 3 to recite "further comprising subjecting the cells to a final aerobic culturing step," which the Examiner has declined to enter.

Claims 1-29 have been rejected for failing to correspond in scope to that which the Applicant regards as his invention, because while the claims recite production of "a bacterium

that contains a single eukaryotic gene," Applicant has asserted during prosecution that the invention relates to "a bacterium that has the phenotype of a prokaryote and the genotype of a eukaryote." Answer, page 11. The Examiner is simply incorrect in asserting that the claims recite production of a bacterium containing just a single eukaryotic gene – they recite a bacterium that contains a eukaryotic and/or viral gene (i.e., at least one gene, either eukaryotic or viral in nature). The claims completely define the invention, because whether or not the resulting bacterium contains one, two, a hundred eukaryotic genes, or an entire eukaryotic genome, it would contain "a eukaryotic and/or viral gene." The statements quoted by the Examiner were made in response to the assertion by the Examiner that a person of ordinary skill in the art would have no way of knowing whether or not the eukaryotic gene in the bacterium produced would be intact. Applicant first pointed that the claim did not require the gene to be intact, and so the observation was misplaced, then went on to note that eukaryotic genes present in the bacteria produced from the claimed methods would be expected to be intact because the current understanding of the mechanism by which the present method operates (expressly set forth in the specification) is that the starting virally-infected eukaryotic cells are essentially converted to what a person having ordinary skill in the art would call "bacteria." The Examiner's comments at best go to the underlying mechanism by which the claimed methods operate, which is irrelevant to determining whether or not the claims particularly point out and distinctly the methods themselves.

Claims 24 and 25 have been rejected for use of the allegedly vague term "derived." The Examiner asserts that it is unclear "what steps are required for this 'derivation,'" and "what are the starting materials." Answer, page 11. In the Applicant's Brief it was pointed out that both claims 24 and 25 expressly incorporate the methods of claims 1 and 15, respectively. Brief, page

23. The Examiner has entirely failed to explain why this express incorporation of the methods by which the claimed cells are "derived" does not particularly point out and distinctly claim the invention. The Examiner only states that claims 1 and 15 "recite open language," without elaborating, and asserts that it is unclear what constitutes a "derived" cell, how said cell differs from a "non-derived cell," or what steps are required for "derivation." Answer, page 25. The claims on their face state that the claimed "derived cell" is (1) pleiomorphic, (2) not a transgenic cell, (3) contains at least one gene evolved from the genome of the eukaryotic cell from which is was derived, and (4) was produced by following the steps recited in claim 1 (in the case of claim 24) or claim 15 (in the case of claim 25). There are thus four objective criteria by which to determine whether or not a particular cell falls within the scope of claim 24 or claim 25. The claims also state on their face how the claimed cells differ from the eukaryotic cells from which they are derived – they have been subjected to the process of either claim 1 or claim 2, and thus are the products of one of those processes – i.e., morphologically resembling a bacterium. The steps required for derivation are also expressly incorporated in the claims – they are the steps of either claim 1 or claim 15. Here again, the Applicant has made a good-faith effort to amend and/or explain the language of claims found by the Examiner to be objectionable, and remains willing to amend the claims further, but the Examiner has hitherto provided no guidance that would assist the Applicant in formulating claim language that would be acceptable.

Claim 24 and 25 have further been rejected for the use of the term "evolved," which the Examiner defines as "to develop or arise through evolutionary processes," which he further asserts are "gradual over time." Answer, page 25. The definition of "evolve" in fact does not carry with it the requirement that the devopment be "gradual over time." See, e.g., Merriam-Webster's Collegiate Dictionary, 10th ed.: "to produce by evolutionary processes ... to undergo

evolutionary change." It means that something has undergone a change from one "thing" to another "thing." Many organisms evolve very quickly even in natural circumstances – bacteria in particular can adapt and change their morphology and genetic make-up very quickly, for example to develop toxin resistance or to adapt to a new environment, as can insects. Genes evolve (change) constantly through mutation, natural recombination, and selection. The Examiner seems to imply that in order for something to be "evolved" it must have developed over a great span of time, like a fish evolving into a mammal, but this simply is not the meaning of the term. Claims 24 and 25 clearly set forth that the claimed cells contain at least one gene that was in the starting eukaryotic cell genome, and has been changed as a result of the process by which the claimed cell was produced (i.e., it "evolved" from the original gene in the starting eukaryotic cell). This term is as precise as the subject matter of the claim permits.

Claims 24 and 25 have further been rejected for the use of the term "pleiomorphic," the Examiner asserting that "it is unclear how the cell of the instant claim differs from any other cell since all cells are pleiomorphic by nature." Answer, pages 11-12. The Examiner defines "pleiomorphic" as "having the ability to change shape." Answer, page 25. As set forth in the Applicant's Brief at pages 21-22, the Examiner is simply wrong that all cells are pleiomorphic by nature. The Examiner offered no response to the Applicant's arguments and supporting evidence. Furthermore, the cells of claims 24 and 25 are defined by several additional criteria, and so are not simply "pleiomorphic," but are defined as the sum of those characteristics. The Examiner's reasoning is no different than rejecting the claims because the term "cell" fails to adequately distinguish the claimed invention. The use of the term "pleiomorphic," per se, cannot render the claim indefinite.

With regard to the Examiner's Answer relating to the term "morphology that is neither prokaryotic nor eukaryotic" (Answer, page 26), Applicants fail to see the distinction that the Examiner is drawing between the description in the specification of the shape (morphology) of the bacteria as opposed to their "overall morphology." As stated in the Applicant's Brief, a person of ordinary skill in the art would have no trouble understanding what is meant by "prokaryotic morphology" versus "eukaryotic morphology" versus morphology that is neither, as there are well-established norms in the art as to the suite of morphological features (of any kind) that characterize a cell as either prokaryotic or eukaryotic, and the combination or spectrum of features is conventionally referred to as the "morphology" of that cell type. Brief, page 22. As explained in the specification, the cells produced by the present invention have "morphologies that appear to be of neither a prokaryotic nor a eukaryotic nature" (e.g., specification at page 29, lines 10-20), which a person having ordinary skill in the art would understand as meaning that they combine features of both, and/or have features that are found in neither, such that their "morphologies" would not be classified as either prokaryotic or eukaryotic. Again, this language is as precise as the subject matter allows.

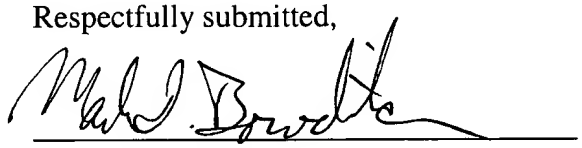
Fifth Issue: With regard to the Examiner's Answer to the Fifth Issue (35 U.S.C. § 112, first paragraph, lack of support), the Examiner asserts that the term "transgenic" used in claims 24-29 applies to "any and all genes of the claimed bacteria not merely the eukaryotic and/or viral genes specifically recited in the claims." Answer, page 26. The Examiner offers no further explanation, or response to the arguments presented in Applicant's Brief, so the Applicant assumes that the Examiner is no longer asserting this grounds for rejection. While heading of the pertinent section of the Appellant's Brief (page 23) does incorrectly refer to the second paragraph of § 112, the Applicant's analysis of the rejection and the relevant law regarding the

written description requirement make clear that this is merely a clerical error. As explained in Applicant's Brief, the Examiner is applying an improper *in haec verba* analysis, as the specification as a whole clearly conveys to a person having ordinary skill in the art that the claimed cells are not "transgenic," because they are not the product of traditional molecular transformation techniques. The Examiner has not explained why "any and all genes of the claimed bacteria" should be considered "transgenic." Applicants note that the Examiner is not asserting that the use of the term renders the claims in question indefinate.

Conclusion

The Examiner's Answer fails to adequately rebut, or in some instances even address, the evidence and arguments presented in the Applicant's Brief. Applicant respectfully submits that, for the reasons set forth in the Applicant's Brief and herein, the final rejections applied to the claims are without merit. Applicant respectfully requests that these rejections be reversed, and that the Board direct the Examiner to issue a favorable action on the claims, or in the alternative, to enter the Applicant's pending amendments to the claims and issue a favorable action on the claims as amended.

Respectfully submitted,



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Mark I. Bowditch
Reg. No. 40,315
114 S. Cherry Street
Falls Church, VA 22046
Tel. (703) 597-8785